PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	§	
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Mummidi, Matthew Dolan and Mike Bamshad	§	
	§	Group Art Unit: Unknown
Serial No.: Unknown	§	
PCT/US00/28158	§	
	§	Examiner: Unknown
Filed: March 29, 2002	§	
Intl. Filing date: October 12, 2000	§	Atty. Dkt.: 4003.001600
Priority date: October 12, 1999	§	
	§	
For: Screening for Disease Susceptibility	§	
By Genotyping the CCR5 and CCR2 Genes	§	

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March 29, 2002
Date

Shelley P.M. Fussey

PRELIMINARY AMENDMENT

BOX PCT
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The present document is a Preliminary Amendment filed in conjunction with the nationalization of International Patent Application PCT/US00/28158. After entry into the U.S. national stage, and assurance of a U.S. filing date, entry of the following amendments is respectfully requested. Any omitted fees are authorized to be deducted from Williams, Morgan & Amerson Deposit Account No. 50-0786/4003.001600.

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Date: March 29, 2002

AMENDMENT

In the Specification:

At page 1, lines 7-11 of the specification, after the title, please delete the existing paragraph and replace with the following paragraph, so that the text reads:

The present application is a nationalization of PCT Application Serial No. PCT/US00/28158, filed October 12, 2000, which claims priority to U.S. provisional application Serial No. 60/159,137, filed October 12, 1999, the entire text, figures and sequences of which applications are incorporated herein by reference without disclaimer. The U.S. government owns rights in the present invention pursuant to grant numbers AI43279 and AI46326 from the National Institutes of Health.

At the end of the specification, after the abstract, please delete the existing pages of sequence listing from the PCT application and replace with the enclosed pages of sequence listing that have been revised to particularly reflect the U.S. national stage.

In the Claims:

After entry into the U.S. national stage, and assurance of a U.S. filing date, please revise the claims from the published PCT application as follows.

Please cancel claims 1-37, without prejudice and without disclaimer.

Please add new claims 38-62, as follows:

38. (New) A set of nucleic acid segments for identifying the CCR5 haplotype group of both alleles of a human subject, wherein said set of nucleic acid segments comprises at least one nucleic acid segment capable of detecting each of the following haplotype groups, each CCR5 haplotype group (haplogroup) being defined in terms of the nucleotides at positions 29, 208, 303,

627, 630, 676 and 927 of the human CCR5 sequence of SEQ ID NO:65, with definition of the amino acid at position 64 and the presence or absence of the Δ32 deletion of the human CCR2 sequence, as follows:

Haplogroup	Nucleotide position in CCR5 sequence							
	29	208	303	627	730	676	927	
HHA:	A	G	G	T	C	A	C	
HHB:	A	T	G	T	C	A	C	
HHC:	A	T	G	T	C	G	C	
HHD:	A	T	G	T	T	A	C	
HHE:	A	G	A	C	C	A	C	
HHF*1:	A	G	A	C	C	A	T	
HHF*2:	A	G	A	C	C	A	T	isoleucine at amino acid 64
HHG*1:	G	G	A	C	C	A	C	
HHG*2:	G	G	A	C	C	A	C	has Δ32, 32 base pair deletion

39. (New) The set of nucleic acid segments of claim 38, further comprising at least one nucleic acid segment capable of detecting a human CCR2 polymorphism at both alleles.

40. (New) The set of nucleic acid segments of claim 39, further comprising at least a first and a second nucleic acid segment that is each capable of detecting a distinct human CCR2 polymorphism at both alleles.

41. (New) The set of nucleic acid segments of claim 38, wherein each of said nucleic acid segments is a primer.

42. (New) A kit comprising a set of nucleic acid segments in accordance with claim 38 and a suitable container for said set of nucleic acid segments.

43. (New) The kit of claim 42, further comprising instructions for identifying the CCR5 haplotype group of both alleles of a human subject and for correlating the haplogroups on both CCR5 alleles with the risk of HIV-1 infection or disease progression in humans.

44. (New) The kit of claim 42, further comprising a restriction endonuclease.

45. (New) The kit of claim 42, further comprising at least one nucleic acid segment capable of detecting a human CCR2 polymorphism at both alleles.

46. (New) The kit of claim 42, further comprising at least a first and a second nucleic acid segment that is each capable of detecting a distinct human CCR2 polymorphism at both alleles.

47. (New) The kit of claim 42, wherein each of said nucleic acid segments is a primer.

48. (New) The kit of claim 42, further comprising at least a first anti-viral therapeutic agent.

49. (New) A method of identifying the CCR5 haplotype group of a human subject, comprising identifying the CCR5 haplotype group of both alleles of a human subject using a set of nucleic acid segments in accordance with claim 38.

50. (New) A method of identifying the CCR5 haplotype group of each member of a cohort of human subjects of a chosen population, comprising identifying the CCR5 haplotype group of both alleles of each member of said cohort of human subjects of said chosen population using a

set of nucleic acid segments in accordance with claim 38 and determining the correlation of said CCR5 haplotype group of both alleles with risk of HIV-1 infection, transmission or disease progression in said population.

51. (New) The method of claim 50, wherein said population is an ethnic group.

52. (New) The method of claim 50, wherein said population is children.

53. (New) The method of claim 50, further comprising identifying the human CCR2 polymorphisms at both alleles and further correlating said CCR2 polymorphisms with risk of HIV-1 infection, transmission or disease progression in said population.

54. (New) A method of assessing the risk of a human subject for HIV-1 infection, transmission or disease progression, comprising identifying the CCR5 haplotype group of both alleles of said human subject using a set of nucleic acid segments in accordance with claim 38, and correlating the pair of haplogroups identified with the risk of HIV-1 infection, transmission or disease progression associated with said pair of haplogroups.

55. (New) The method of claim 54, wherein said pair of haplogroups identified for the human subject is correlated with the risk of HIV-1 infection, transmission or disease progression associated with that pair of haplogroups for a population to which the subject belongs.

56. (New) The method of claim 54, wherein said human subject is Caucasian and the presence of two HHE alleles is indicative of an increased risk of HIV-1 infection or disease progression.

57. (New) The method of claim 54, wherein said human subject is African-American and the presence of an HHC and an HHF*1 haplogroup, an HHC and an HHE haplogroup, two HHC haplogroups, or an HHC and an HHD haplogroup is indicative of an increased risk of HIV-1 infection or disease progression.

58. (New) The method of claim 54, wherein said human subject is a child and the presence of an HHC and an HHE haplogroup, two HHE haplogroups, or an HHE haplogroup and an HHG*2 haplogroup is indicative of an increased risk of HIV-1 transmission, infection or disease progression.

59. (New) The method of claim 54, wherein a human subject identified as having an increased risk of HIV-1 infection or disease progression is treated with a biologically effective amount of at least a first anti-viral agent.

60. (New) A method of reducing HIV-1 infection, transmission or disease progression in a human subject, comprising:

(a) identifying a susceptible human subject by:

(i) identifying the CCR5 haplotype group of both alleles of said human subject using a set of nucleic acid segments in accordance with claim 38; and

(ii) correlating the pair of haplogroups identified with the risk of HIV-1 infection, transmission or disease progression associated with said pair of haplogroups; and

(b) treating said susceptible human subject with a biologically effective amount of at least a first anti-viral agent.

61. (New) A nucleic acid segment for identifying a CCR5 haplotype group of a human subject, which nucleic acid segment is capable of detecting the human haplotype group HHD, which has nucleotide A at position 29, T at position 208, G at position 303, T at position 627, T at position 630, A at position 676 and C at position 927 of the human CCR5 sequence of SEQ ID NO:65.

62. (New) The nucleic acid segment of claim 61, comprised within a set of nucleic acid segments for identifying the CCR5 haplotype group of both alleles of a human subject.

REMARKS

I. Nationalization

This application represents the U.S. national stage under 35 U.S.C. § 371 of International Patent Application PCT/US00/28158, filed October 12, 2000, which claims priority to U.S. provisional application Serial No. 60/159,137, filed October 12, 1999.

As the text of the International Application was filed with the U.S. receiving office, an additional copy is not required to satisfy 35 U.S.C. § 371(c)(2). Other than the inventors, sequence listing and claims (see below), the application was not amended during the PCT phase.

Priority to the earlier provisional application was already properly claimed at page 1 of the specification. As a precaution, a further amendment is being made to page 1 of the specification to positively recite that this application is a nationalization of the PCT Application.

II. Inventorship

The inventors of the present application are Sunil Ahuja, Enrique Gonzalez, Srinivas Mummidi, Matthew J. Dolan and Mike Bamshad.

The correct spelling of two of the originally listed inventors' names is: Srinivas Mummidi (not Srivinas) and Enrique Gonzalez (not Gonzales). These corrections were made during the PCT phase under Rule 92*bis*.

Matthew J. Dolan and Mike Bamshad were added as inventors during the PCT phase to correct an inadvertent error upon filing. The error was made without deceptive intent on the part of Matthew J. Dolan and Mike Bamshad, and without deceptive intent on the part all others concerned with this application.

III. International Preliminary Examination Report

The PCT application underwent Chapter II examination, using the European Patent Office (EPO) as the International Searching and Examination Authority (ISA/IEA). The international search and examination both determined that all claims were drawn to a unified inventive concept.

At the stage of the International Preliminary Examination Report (IPER), revised claims 1-23 were pending in the PCT application. The IPER determined each of claims 1 and 3-23 to be novel and inventive (copy of IPER enclosed as **Exhibit A**). Applicants therefore elect to enter the U.S. national stage using a set of claims based upon claims 1 and 3-23 from the IPER stage, but revised to correct informalities and better accord with U.S. practice.

IV. National Stage Claims

Amendments were made to the claims in the PCT application during Chapter II examination. Such claim amendments should not be entered upon entry into the U.S. national stage. The original, unamended PCT application therefore forms the basis for the amendments introduced herein.

After according a U.S. filing date, and before calculating the filing fee, entry of the foregoing claim amendments is respectfully requested. The present claims are fully supported by the specification and claims of the PCT and priority application and do not in any way constitute new matter.

The submission of new claims does not represent abandonment of any of the subject matter of the claims in the PCT application. In fact, the new claims are intended to represent those at the IPER stage, of which claims 1 and 3-23 satisfied the requirements for novelty and inventive step.

The changes to the claims mainly correct informalities and remove multiply dependencies, to accord with U.S. procedures and to avoid multiply-dependent and excess claim fees. Other minor changes are introduced at certain points, to better accord with U.S. practice.

V. Status of the Claims

The PCT application was filed with claims 1-37. During Chapter II examination before the EPO, revised claims 1-23 were submitted, but are not of record in the United States. Presently, claims 1-37 have been cancelled, entirely without prejudice or disclaimer. Claims 38-62 have been added, which are fully supported by the specification and correlate with claims 1 and 3-23 from the IPER stage. The new claims are being submitted to correct informalities, remove multiply dependencies and to better accord with U.S. practice.

Claims 38-62 are therefore in the case. In accordance with 37 C.F.R. § 1.121, and for the convenience of the Examiner, a clean copy of the pending claims is included herewith as **Exhibit B**. As there have been no changes to previous claims, only additions, another claim exhibit is not necessary.

VI. Support for the Claims

Current claims 38-62 are based upon claims 1 and 3-23 from the IPER stage. As the claims have been re-numbered, the dependencies changed and minor reorganization has been implemented, Applicants are providing a table so that the examiner can readily correlate the present claims with those from the IPER stage (**Exhibit C**).

Support for claims 38-62 in claims 1 and 3-23 from the IPER stage is apparent in the first two columns of the table (**Exhibit C**). Support for IPER claims 1-23 was detailed during PCT examination. For the convenience of the examiner, the additional support for the claims in the specification has been added to the last column of the table (**Exhibit C**).

It will therefore be understood that no new matter is encompassed by any of the present claims.

VII. The Claims are Allowable

The present claims define sets of nucleic acid segments that are capable of identifying defined human CCR5 haplogroups, kits containing those nucleic acid segments and methods for identifying human CCR5 haplogroups using such nucleic acid segments. Methods for correlating pairs of human CCR5 haplogroups with risk of HIV-1 infection, transmission or disease progression in chosen populations are also presented, as are methods for assessing the risk to individuals of HIV-1 infection, transmission or disease progression using the correlations obtained for populations.

The IPER issued in the PCT application determined that each of claims 1 and 3-23 were novel and inventive (**Exhibit A**). Current claims 38-62 (**Exhibit B**) are based upon claims 1 and 3-23 from the IPER stage, but have been revised to correct informalities, remove multiply dependencies and comply with U.S. procedures (**Exhibit C**).

The few remaining issues and informalities listed in the IPER are either addressed herein or were unique to the EPO. Claim 2 has been canceled; claim 23 complies with U.S. statutes; claim 1 has been revised to correct an informality in reference to amino acid position 64 and the presence or absence of the Δ32 deletion as pertaining to the human CCR2 gene sequence; and claim 13 refers to the set of nucleic acid segments of the first independent claim. The comments on the number of independent claims are not applicable to the United States, but Applicants have nonetheless streamlined the present claims.

In light of the IPER and the foregoing comments, Applicants respectfully submit that the present claims have utility and define with clarity a unified, novel and non-obvious invention that is supported by an enabling specification. Applicants therefore urge that the present claims be directly progressed to allowance, and such action is respectfully requested.

VIII. Specification and Sequence Listing

The proper claim for priority has been timely introduced into the specification by amendment of the opening paragraph at page 1, in accordance with 37 C.F.R. § 1.121. This is proper as the amendment includes the reference, replacement paragraph in clean form and another version of the replacement paragraph separate from the amendment marked up to show all changes **(Exhibit D)**.

A sequence listing particularly adapted for the U.S. national stage is also enclosed **(Exhibit E)**. The sequence listing has been introduced into the specification by amendment of the pages after the abstract. Other than including the priority applications, U.S. filing date and complying with the procedural requirements of the sequence listing rules, the sequence listing contains no changes.

It will thus be understood that no new matter is included within the amendments to the specification.

IX. Fees and Formalities

The national filing fee and claim fees are included herewith. The fees have been calculated after the present changes to the claims. Any omitted fees should be deducted from Williams, Morgan & Amerson Deposit Account No. 50-0786/4003.001600. Applicants are entitled to small entity status. A verified statement to this effect is no longer required.

The requirements for formal drawings were met in the PCT stage. However, additional formal drawings are enclosed herewith as a precaution.

The sequence listing requirements were also met in the PCT stage. As the sequence listings from PCT applications do not appear to be made of record in U.S. national stage

applications, a sequence listing particularly adapted for the U.S. national stage has been generated and is enclosed. A sequence listing diskette, two hard copies of the sequence listing and a verified statement are all enclosed.

X. Conclusion

In conclusion, Applicants submit that, in light of the finding of the IPER, the present claims define a unified invention that is in condition for allowance, and an early indication to this effect is respectfully requested. Should the Examiner have any questions or comments, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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